

Case T-P10-203
754,032

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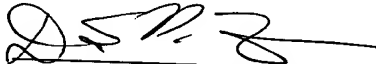
Applicants respectfully request that the Examiner consider the listed documents and indicate that they were considered by making appropriate notations on the attached Form PTO-1449.

This submission does not represent that a search has been made or that no better art exists. Nor does it constitute an admission that each or all of the listed documents are material or constitute "prior art." If the Examiner applies any of the documents as prior art against any claim in the application and applicants determine that the cited documents do not constitute "prior art" under United States law, Applicants reserve the right to present to the Office the relevant facts and law regarding the appropriate status of such documents.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

If there are any fees due in connection with the filing of this Statement, please charge the fees to our **Deposit Account, No. 18-1945.**

Respectfully submitted,
Ropes & Gray

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U.S. PATENT DOCUMENTS

EXAMINER INITIALS	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
AB	5798209	25-Aug-1998	Chan	435	6	26-May-1995
AB	5837538	17-Nov-1998	Scott	435	325	06-Oct-1995
AC	5935810	10-Aug-1999	Friedman et al.	435	69.1	30-Nov-1994

FOREIGN PATENT DOCUMENTS

DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	Translation	
					YES	NO
AD	WO9611260	18-Apr-1996	PCT	C12N	5/00	

OTHER DOCUMENTS

(Including Author, Title, Date, Pertinent Pages Etc.)

AE	Akimaru, H. et al., "Drosophila CBP is a co-activator of cubitus interruptus in hedgehog signaling", Nature 386 (6626): 735-738 (1997).
AF	Akiyama, H. et al., "Cloning of a mouse smoothened cDNA and expression patterns of hedgehog signaling molecules during chondrogenesis and cartilage differentiation in conal mouse EC cells, ATDC5", Biophys Res. Comm., 235(1): 142-147 (1997).
AG	Alberts, eds., Molecular Biology of the Cell, G-10 (1994).
AH	Alcedo, J. et al., "The Drosophila smoothened gene encodes a seven-pass membrane protein, a putative receptor for the hedgehog signal", Cell, 86 (2): 221-232 (1996).
AI	Alcedo, J. and Noll, M., "Hedgehog and its patched-smoothened receptor complex: a novel signaling mechanism at the cell surface", Biol. Chem., 378 (7): 583-590 (1997).
AJ	Alexandre, C. et al., "Transcriptional activation of hedgehog target genes in Drosophila is mediated directly by the cutitus interruptus protein, a member of the GLI family of zinc finger DNA-binding proteins", Genes Dev., 19 (16): 2003-2013 (1996).
AK	Bale, A., "Variable expressivity of patched mutations in flies and humans", Am. J. Human Genet., 60 (1): 10-12 (1997).
AL	Bellusci, S. et al., "Involvement of Sonic hedgehog (Shh) in mouse embryonic lung growth and morphogenesis", Development, 124 (1): 53-63 (1997).
AM	Bhat, K. and Schedl, P., "Requirement for engrailed and invected genes reveals novel regulatory interactions between engrailed/invected, patched, gooseberry and wingless during Drosophila neurogenesis", Development, 124 (9)L 1675-1688 (1997).
AN	Bitgood, M. et al., "Sertoli cell signaling by Desert hedgehog regulates the male germline", Curr. Biol., 6 (3): 298-304 (1996).
AO	Bokor, P. et al., "The roles of hedgehog, wingless and lines in patterning the dorsal epidermis in Drosophila", Development, 122 (4): 1083-1092 (1996).
AP	Bowie et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions", Science 247: 1306-1310 (1990).

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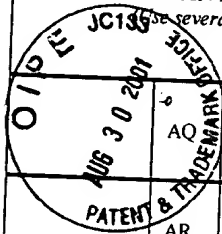
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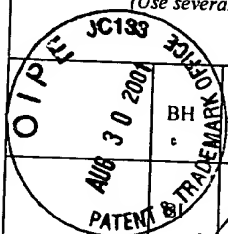
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	BJ	Grindley, J. et al., "Evidence for the involvement of the Gli gene family in embryonic mouse lung development", Dev. Biol., 188 (2): 337-348 (1997).
	BK	Habuchi, et al., "Detailed deletion mapping of chromosome 9q bladder cancer: evidence of two tumour suppressor loci", Oncogene, 11:1671-1674 (1995).
	BL	Hahn, H. et al., "A mammalian patched homolog is expressed in target tissues of sonic hedgehog and maps to a region associated with development abnormalities", J. Biol. Chem., 271 (21): 12125-12128 (1996).
	BM	Heemskerk, J. et al., "Drosophila hedgehog acts as a morphogen in cellular patterning", Cell 76: 449-460 (1994).
	BN	Hepker, J. et al., "Drosophila cubitus interruptus forms a negative feedback loop with patched and regulates expression of Hedgehog target genes", Development, 124 (2): 549-558 (1997).
	BO	Hidalgo, A. and Ingham, P., "Cell patterning in the Drosophila segment: spatial regulation of the segment polarity gene patched", Development, 110: 291-301 (1990).
	BP	Hooper et al., "The Drosophila patched gene encodes a putative membrane protein required for segmental patterning", Cell 59: 751-765 (1989).
	BQ	Hynes, M., et al., "Control of cell pattern in the neural tube by zinc finger transcription factor and oncogene _____ Neuron 19(1): 1997).
	BR	Ingham, "Hedgehog points the way", Curr. Biol. 4: 347-350 (1994).
	BS	Ingham, P. et al., "Role of the Drosophila patched gene in positional signalling", Nature, 353: 184-187 (1991).
	BT	Ingham, P. et al., "Quantitative effects of hedgehog and decapentaplegic activity on the patterning of the Drosophila wing", Curr. Biol., 5 (4): 432-440 (1995).
	BU	Jensen, A. et al., "Expression of Sonic hedgehog and its putative role as a precursor cell mitogen in the developing mouse retina", Development, 124 (2): 363-371 (1997).
	BV	Jiang, J. et al., "Protein kinase A and hedgehog signaling in Drosophila limb development", Cell, 80 (4): 563-572 (1995).
	BW	Johnson, R. et al., "Patched overexpression alters wing disc size and pattern: transcriptional and post-transcriptional effects on hedgehog targets", Development, 121 (12): 4161-4170 (1995).
	BX	Johnson, R. et al., "Human homolog of patched, a candidate gene for the basal cell nevus syndrome", Science, 272 (5268): 1668-1671 (1996).
		Kalderon, D., "Morphogenetic signalling. Responses to hedgehog", Curr. Biol., 5 (6): 2279-2289 (1995).

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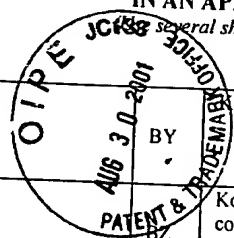
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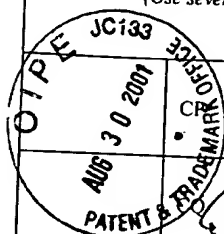


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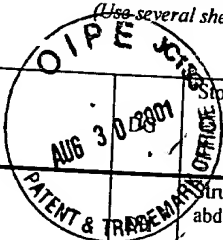
		Pennisi, "Gene Linked to Commonest Cancer", Science 272: 1583-1584 (1996).
		Perrimon et al., "Generating lineage-specific markers to study Drosophila development", Dev. Genet. 12:238-252 (1991).
	CR	Perrimon, N., "Serpentine proteins litter into the wingless and hedgehog fields", Cell, 86 (4): 513-516 (1996).
	CS	Phillips, R. et al., "The Drosophila segment polarity gene patched is involved in a position signalling mechanism in imaginal discs", Development, 110: 105-114 (1990).
	CT	Quinn, A. et al., "Chromosome 9 allele loss occurs in both basal and squamous cell carcinomas of the skin", J. Invest. Dermatology, 102: 300-303 (1994).
	CU	Quinn, A. et al., "Delineation of two distinct deleted regions on chromosome 9 in human non-melanoma skin cancers", Genes, Chromosomes & Cancers, 11:222-225 (1994).
	CV	Riddle, R. et al., "Sonic hedgehog mediates the polarizing activity of the ZPA", Cell, 75: 1401-1416 (1993).
	CW	Roelink, H. et al., "Floor plate and motor neuron induction by <i>vhh-1</i> , a vertebrate homolog of hedgehog expressed by the notochord", Cell, 76: 761-775 (1994).
	CX	Rogers, G. et al., "Patched gene mutation screening in patients with basal cell nevus syndrome using bidirectional dideoxy fingerprinting", J. Invest. Dermatol. Abstracts, 108(4): 598, # 364, (1997).
	CY	Roush, W., "Hedgehog's patterning call is patched through, smoothly", Science, 274 (5291): 1304-1305 (1996).
	CZ	Sanicola, M. et al., "Drawing a stripe in Drosophila imaginal disks: negative regulation of decapentaplastic and patched expression by engrailed", Genetics, 139 (2): 745-756 (1995).
	DA	Schuske, K. et al., "Patched overexpression causes loss of wingless expression in Drosophila embryos", Dev. Biol., 164 (1): 300-301 (1994).
	DB	Shilo, B., "Tumor suppressors. Dispatches from patched", Nature, 382 (6587): 115-116 (1996).
	DC	Simcox, A. et al., "Imaginal discs can be recovered from culture embryos mutant for the segment-polarity genes engrailed, naked and patched but not from wingless", Development, 107: 715-722 (1989).
	DD	Sisson, J. et al., "Costal2, a novel kinesin-related protein in the Hedgehog signaling pathway", Cell, 90 (2): 235-245 (1997).
	DE	Smith et al., "Genes Transferred by Retroviral Vectors into Normal and Mutant Myoblasts in Primary Cultures Are Expressed in Myotubes", Mol. Cell. Biol. 3268-3271 (1990).
	DF	Spradling et al., "Transposition of Cloned P Elements into <i>Drosophila</i> Germ Line Chromosomes", Science 218: 341-347 (1982).

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EXAMINER

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